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09/229,226	01/12/1999	JIN LIU	GTRC-1957	7360

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PATREA L. PABST
HOLLAND & KNIGHT LLP
SUITE 2000, ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET, N.E.
ATLANTA, GA 30309-3400

EXAMINER

SMITH, RUTH S

ART UNIT	PAPER NUMBER
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24

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 24

Application Number: 09/229,226
Filing Date: January 12, 1999
Appellant(s): LIU ET AL.

MAILED

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GROUP 3700

Holland & Knight LLP
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 18, 2003.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

Appellant's brief includes a statement that claims 1-33 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

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5,445,611	Eppstein et al	8-1995
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5,636,632	Bommannan et al	6-1997
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Tachibana et al, "Albumin Microbubble EchoContrast material as an Enhancer for Ultrasound Accelerated Thrombolysis", Circulation, vol 92 (1995), pp 1148-1150

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

Claims 1-25,27-33 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is vague and indefinite in that it is unclear as to how the step set forth on lines 3-4 differs from the step set forth in claim 27, lines 4-5. It appears that such a step is redundant in view of the limitation set forth in claim 27. The preamble of claim 1 is inconsistent with the preamble of claim 27. Claim 27 is vague and indefinite in that reference to a different tissue on line 7 implies that a first tissue has been previously set forth, however, such a term lacks antecedent basis in that the preamble refers to tissue in the alternative only. Claims 31-33 appear to be inconsistent with the limitation set forth in claim 27 regarding applying the transducer to a site other than where transport or cell viability is to be altered. Placement of the transducer in the body would cause direct application of the acoustic energy to the treatment site rather than the remote application as set forth in claim 27.

Claim Rejections - 35 USC § 102

Claims 1-2,10,11,14,15,17,19,21,23-28 have been rejected under 35 U.S.C. 102(e) as being clearly anticipated by Klopotek (6,113,559). The claims are directly readable on Klopotek which discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. The

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ultrasound is applied to the other layers of skin and affect cells in the underlying layers of skin. Klopotek discloses altering cell viability in the dermis and because skin is an organ, the dermis is considered to be an internal organ, internal tissue and include blood vessels. The acoustic energy is applied to the stratum corneum which defines a site other than where the cell viability is to be altered. The underlying layers of skin are considered to be different tissue at a second distant site. With regard to claims 19,21, the feedback signals used regarding cavitation are measured at frequencies as set forth in the claims.

Claims 27-28,30 have been rejected under 35 U.S.C. 102(b) as being anticipated by Eppstein et al. The claims are directly readable on Eppstein et al which disclose the use of ultrasound energy to alter transport of agents into the body. The frequency can be changed such that the energy is directed to a deeper part of the tissue. Therefore, the energy is administered at the stratum corneum by a transducer placed thereon and the energy alters transport and cell viability at a site distant from the layer of skin on which the transducer is placed. The site distant from the layer of skin on which the transducer is placed comprises the dermis or other tissues beneath it which therefore comprises different tissue (see column 9, lines 33-46). Skin is an organ, therefore, the dermis is considered to be an internal organ, internal tissue and include blood vessels.

Claim Rejections - 35 USC § 103

Claim 22 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Klopotek ('559). Klopotek discloses using a feedback system to modify continued application of ultrasound for the treatment of tissue. The feedback system measures properties such as ultrasound energy levels, temperature etc. In the absence of any showing of criticality, the means used to analyze the energy measurements would have been an obvious design choice of known equivalents in the art.

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Claims 1-5,8-18,23-26,29 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Eppstein et al in view of Klopotek ('559). Eppstein et al disclose administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The frequency and/or intensity can be selected based upon the drug administered, and the disease or injury treated. The site distant from the layer of skin on which the transducer is placed comprises the dermis or other tissues beneath it which therefore comprises different tissue (see column 9, lines 33-46). Skin is an organ, therefore, the dermis is considered to be an internal organ, internal tissue and include blood vessels. Klopotek discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have provided a feedback system as taught by Klopotek in order to avoid transmitting excessive waves through the patient. With respect to claim 3, the agent passed through the membrane would have been an obvious selection based upon the intended treatment, and in the form of an emulsion or liposome as is well known. With regard to claim 9, it appears that such is an inherent function of the method. With regard to claims 13,29, it appears that the method of Eppstein et al would be applicable to any type of biological membrane and to any type of cell. With regard to claim 14, Eppstein et al disclose a frequency in the range of .1-100MHz. With respect to claim 16, in the absence of any showing of criticality, the peak positive pressure used would have been obvious to one skilled in the art without undue experimentation in order to achieve the desired result. With regard to claim 17, the step is an inherent result of the method. With regard to claims 23,24, the frequency and device location can be changed depending upon the procedure being performed.

Claim 1-3,5,7,14,15,18,23,25-27 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Tachibana et al in view of Klopotek ('559). Tachibana et al disclose the use of low-level ultrasound to alter cell viability. The ultrasound is administered for a predetermined time period after which it is terminated. The

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ultrasound is administered at one site and used to alter cell viability in an organ that includes a tumor. The intensity was varied over time and the ultrasound was used to kill cells. The ultrasound was applied at a frequency of 270 KHz and used with agent such as Photofrin II. Klopotek discloses using a feedback system to modify continued application of low-level ultrasound for the treatment of tissue. Klopotek uses a non-invasive ultrasound device that is placed against the skin to apply ultrasound to underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have modified Tachibana et al such that it includes a non-invasive low-level ultrasound device and a feedback system as taught by Klopotek in order to ensure that the treatment is being performed as desired and without causing harm to the patient. The use of the device as disclosed by Klopotek involves the selection of a well known ultrasound device for in-vivo low-level ultrasonic treatment.

Claim 6 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Epstein et al in view of Klopotek and Bommannan et al. Epstein et al disclose administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The frequency and/or intensity can be selected based upon the drug administered, and the disease or injury treated. The site distant from the layer of skin on which the transducer is placed comprises the dermis or other tissues beneath it which therefore comprises different tissue (see column 9, lines 33-46). Skin is an organ, therefore, the dermis is considered to be an internal organ, internal tissue and include blood vessels. Klopotek discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have provided a feedback system as taught by Klopotek in order to avoid transmitting excessive waves through the patient. With respect to claim 3, the agent passed through the membrane would have been an obvious selection based upon the intended treatment, and in the form of an emulsion or liposome as is well known. Bommannan et al disclose administering

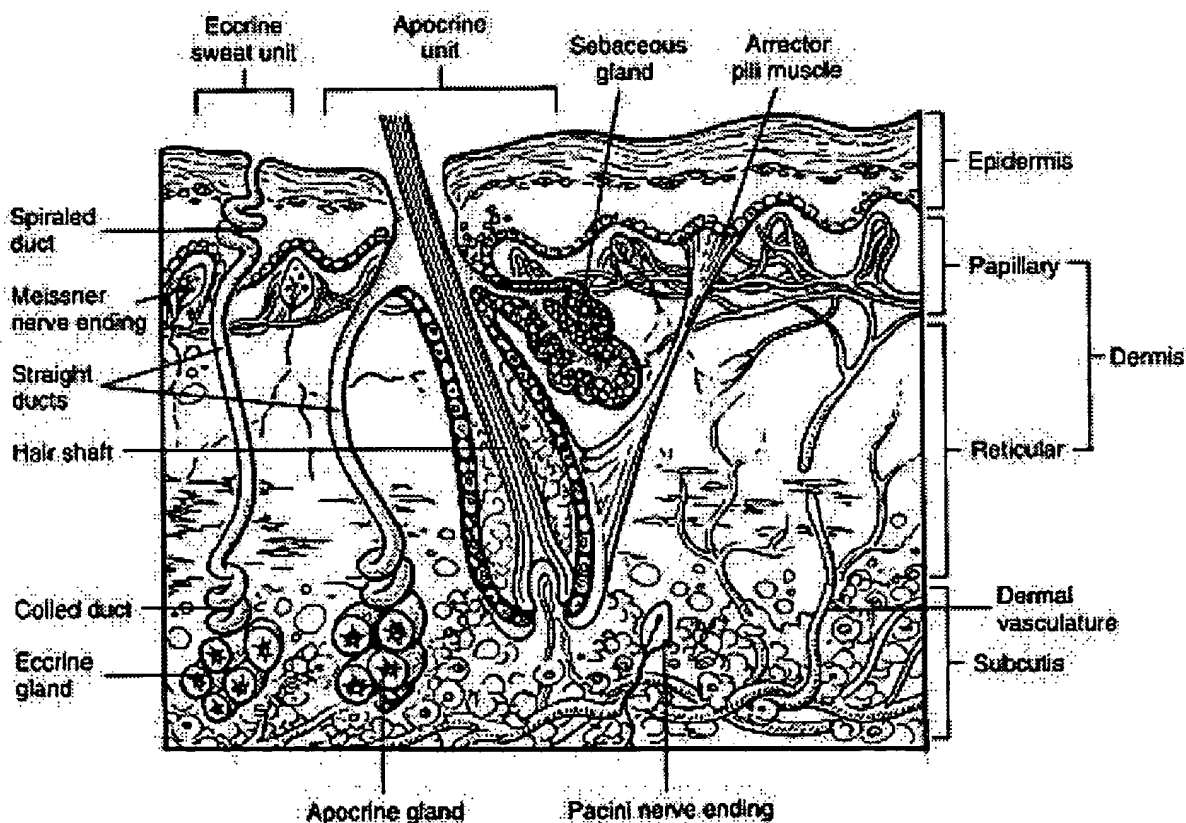
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acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The energy is administered for a time period which can be selected based upon the drug administered, and the disease or injury treated (see column 7, lines 6-10). The measurement of the time that the ultrasound is applied is a measurement of a property of the acoustic energy. Bommannan et al further disclose that the method can be used to sample and evaluate biological fluids in the body (see column 4, lines 55-59). It would have been obvious to one skilled in the art to have further modified Eppstein et al such that in addition to transporting drugs into the body, the ultrasound is selected to enhance the transdermal molecular flux rate out of the human body and used to evaluate biological fluids in the body. The advantage of such is to monitor the effect of the drug treatment.

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(11) Response to Argument

Regarding the appellant's arguments concerning whether the skin as a whole should be considered one tissue, it is respectfully submitted that 1) the claims do not refer to different tissue types but rather different tissues and 2) even assuming that one were to interpret the claims as defining different tissue types, given the figure shown below, the different layers of skin clearly define different tissue types in that the dermis includes blood vessels and nerve cells that are not found in the epidermis which includes as an outer layer the stratum corneum.



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For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,



Ruth S Smith
Primary Examiner
Art Unit 3737

RSS
May 14, 2003

Conferees



JOHN P. CALVERT
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 3700

PATREA L PABST
HOLLAND & KNIGHT LLP
ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET, SUITE 2000
ATLANTA, GA 30309-3400